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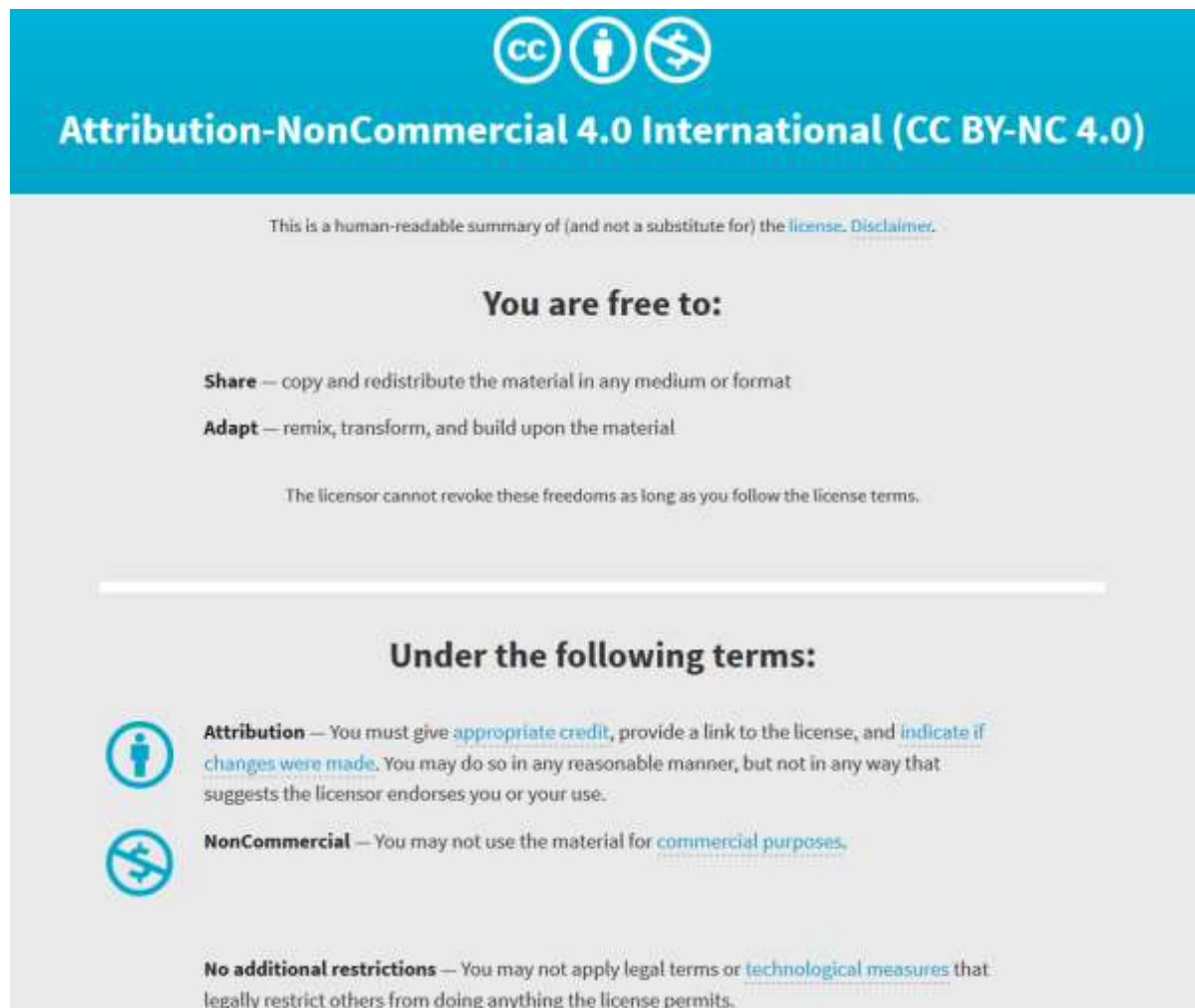
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Thrombelastography in Horses with Acute Gastrointestinal Disease

K.L. Epstein, B.M. Brainard, S.E. Gomez-Ibanez, M.A.F. Lopes, M.H. Barton, and J.N. Moore

Background: Coagulopathies in horses with gastrointestinal disease are frequently identified and associated with morbidity and fatality.

Objective: Determine if thrombelastography (TEG) identifies abnormalities associated with lesion type, presence of systemic inflammatory response syndrome (SIRS), morbidity, and fatality more consistently than traditional coagulation testing.

Animals: One-hundred and one horses examined for gastrointestinal disease and 20 healthy horses.

Methods: TEG, tissue factor (TF)-TEG, and traditional coagulation panels parameters and percentages of horses with coagulopathies were compared for lesion type, presence of SIRS, complications, and survival.

Results: Changes in individual parameters and increased incidence of coagulopathies were associated with fatality (R, $P = .007$; k-value [K], $P = .004$; clot lysis [CL]30, $P = .037$; CL60, $P = .050$; angle [Ang], $P = .0003$; maximum amplitude [MA], $P = .006$; lysis [Ly]30, $P = .042$; Ly60, $P = .027$; CI, $P = .0004$; ≥ 2 TEG coagulopathies, $P = .013$; ≥ 3 TEG coagulopathies, $P = .038$; TF-R, $P = .037$; TF-K, $P = .004$; TF-CL30, $P < .0001$; TF-CL60, $P < .0001$; TF-Ang, $P = .005$; TF-Ly30, $P = .0002$; TF-Ly60, $P < .0001$; TF-CI, $P = .043$; ≥ 1 TF-TEG coagulopathies, $P = .003$; ≥ 2 TF-TEG coagulopathies, $P = .0004$; prothrombin time [PT], $P < .0001$; activated partial thromboplastin time [aPTT], $P = .021$), inflammatory lesions (MA, $P = .013$; TF-CL30, $P = .033$; TF-CL60, $P = .010$; TF-Ly60, $P = .011$; ≥ 1 TF-TEG coagulopathy, $P = .036$; ≥ 2 TF-TEG coagulopathy, $P = .0007$; PT, $P = .0005$; fibrinogen, $P = .019$), SIRS (MA, $P = .004$; TF-CL30, $P = .019$; TF-CL60, $P = .013$; TF-Ly30, $P = .020$; TF-Ly60, $P = .010$; PT, $P < .0001$; aPTT, $P = .032$; disseminated intravascular coagulation, $P = .005$), and complications (ileus: aPTT, $P = .020$; diarrhea: TF-CL30, $P = .040$; TF-Ly30, $P = .041$; thrombophlebitis: ≥ 1 TF-TEG coagulopathy, $P = .018$; laminitis: MA, $P = .004$; CL60, $P = .045$; CI, $P = .036$; TF-MA, $P = .019$; TF-TEG CI, $P = .019$). Abnormalities in TEG and TF-TEG parameters were indicative of hypocoagulation and hypofibrinolysis.

Conclusions and Clinical Importance: TEG identifies changes in coagulation and fibrinolysis associated with lesion type, SIRS, morbidity, and fatality in horses with gastrointestinal disease.

Key words: Coagulopathy; Point-of-care coagulation testing; Viscoelastic coagulation testing.

Coagulopathies are common in horses with gastrointestinal disease, because systemic inflammatory responses can activate coagulation.¹ Abnormalities in a variety of tests evaluating coagulation times, markers of recent coagulation, and anticoagulant factors, in addition to factors associated with fibrinolysis or inhibition of fibrinolysis are identified and associated with morbidity and case fatality rate.^{2–19} Horses with gastrointestinal disease, especially severe disease, have evidence of recent coagulation and fibrinolysis with concurrent evidence of decreased procoagulant and profibrinolytic factors.^{2–4,7,8,12–15,17–19} These changes are consistent with activation and subsequent consumption of coagulation and fibrinolytic factors. Once evidence of consumption is present, conventional testing cannot determine the balance between activation and consumption, and thus, whether a horse is hyper- or hypocoagulable and hyper- or hypofibrinolytic.

Abbreviations:

Ang	angle
aPTT	activated partial thromboplastin time
AT	antithrombin
CL	clot lysis
DIC	disseminated intravascular coagulation
FDP	fibrin degradation products
I	inflammatory
K	k value
Ly	lysis
MA	maximum amplitude
NSM	nonstrangulating medical
NSS	nonstrangulating surgical
PT	prothrombin time
R	reaction time
S	strangulating
TEG	thrombelastography
TF	tissue factor

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Thrombelastography (TEG) is a whole-blood, point-of-care coagulation assay that provides information on the kinetic and mechanical properties of a clot as it forms, matures, and undergoes fibrinolysis. The use of whole blood allows evaluation of cellular and plasma components of coagulation concurrently, whereas typical coagulation tests only assess alterations in plasma components. TEG might offer a more complete picture of the balance of coagulation in individual animals by providing a global assessment of coagulation. TEG has been used to assess coagulopathies (hyper- and hypocoagulable states) in humans and animals.^{20–24} Reference ranges for TEG in healthy horses with and without the addition of tissue factor (TF) have been established.^{25–27}

Measured TEG parameters include reaction time (R; time to the clot initiation), k value (K; the time for the tracing to achieve a set clot strength), angle (Ang; the rate of clot formation), and maximum amplitude (MA; the greatest clot strength).²⁰ Hypercoagulability is characterized by decreases in R and K and increases in Ang and MA, while hypocoagulability results in the opposite. TEG parameters that assess fibrinolysis include clot lysis (CL30 and CL60; percent of MA at 30 and 60 minutes after reaching MA) and lysis (Ly30 and Ly60; percent decrease in area under the curve compared with MA at 30 and 60 minutes).²⁰ Hyperfibrinolysis results in decreased CL and increased Ly, while hypofibrinolysis results in the opposite. TEG performed in a limited number of horses with gastrointestinal disease demonstrates both hypercoagulability or hypocoagulability.^{a,27} These results suggest that TEG might be helpful in determining where a horse stands on the continuum between activation and consumption of coagulation and fibrinolytic factors.

The objectives of this study were to identify relationships between admission TEG and type of gastrointestinal lesion, presence of systemic inflammatory response syndrome (SIRS), morbidity (ileus, diarrhea, fever, thrombophlebitis, and laminitis), and fatality in horses with gastrointestinal disease. Additionally, the relationships were compared with those identified with a traditional coagulation panel. These objectives were formulated to test the hypotheses that abnormalities detected on admission TEG would be associated with lesion type, presence of SIRS, morbidity, and fatality, and that TEG performed with or without TF would identify these associations more consistently than traditional coagulation testing.

Materials and Methods

Study Population

This study was a prospective clinical evaluation. Adult horses (>1 year) admitted to the University of Georgia Veterinary Teaching Hospital between July 2007 and July 2008 for emergency evaluation of gastrointestinal disease were eligible for inclusion. The study was approved by the Institutional Animal Care and Use Committee of the University of Georgia and written informed consent for study participation was obtained from all owners.

Blood samples were obtained within 2 hours of admission. Horses that had received blood products or synthetic colloids as part of initial therapy in hospital or before referral were excluded because of the potential for interactions with coagulation. Analysis of medical records was performed once horses were discharged or euthanized.

Sampling Technique

Whole blood was collected by an experienced veterinarian via clean jugular venipuncture. The jugular vein used had no indwelling catheter in place and was free of palpable or visible evidence of thrombus, phlebitis, or thrombophlebitis. A 19G 3/4 in. butterfly catheter^b was used to collect the blood into a syringe.^c Blood was then transferred with a fresh 18G 1 in. needle to 4 vacuum-evacuated tubes containing 3.2% citrate,^d resulting in a final citrate: blood ratio of 1:9 (TEG, prothrombin time [PT], activated partial thromboplastin time [aPTT], fibrinogen, antithrombin [AT], \pm platelet count), and 1 vacuum-evacuated tube containing soy trypsin (fibrin degradation products [FDP]).^d

TEG

TEG was performed with 2 channels of a thrombelastograph^e with (TF-TEG) and without (TEG) TF activation as described previously.²⁵ Output of the TEG was recorded on a desktop computer by the TEG Analytical software.^f Clotting index (CI) is a parameter that can be calculated from measured TEG parameters (R, K, Ang, and MA) to estimate the overall tendency of the patient to be hyper- (increase) or hypocoagulable (decrease). CI was calculated as $0.1227R + 0.0092K + 0.1655MA - 0.0241Ang - 5.022$.²⁰

Coagulation Profile

Coagulation profiles included PT, aPTT, platelet count, AT, fibrinogen, and FDP. Platelet counts were performed as part of a CBC^g during the routine clinical evaluation of client-owned animals. If thrombocytopenia was detected, the platelet count was repeated on a citrated sample to rule out EDTA-induced pseudothrombocytopenia.^{h,28} Citrated samples for PT, aPTT, fibrinogen, and AT were centrifuged immediately after collection at $1,500 \times g$ for 10 minutes at 4°C. Plasma was harvested and frozen at -80°C before batch analysis. The PT, aPTT, and fibrinogen analyses were performed with optical measurement techniques.ⁱ AT was assayed using a chromogenic assay.^j The tube containing soy trypsin sat at room temperature for 1 hour, and was then centrifuged at $1,500 \times g$ for 10 minutes at 4°C. The serum was collected and frozen at -80°C until batch analysis. FDP concentrations were measured by a semi-quantitative latex agglutination technique.^k

Coagulopathy

Twenty healthy, adult, university-owned horses were sampled as described for the study population to establish reference values. Study horses were defined as having a coagulopathy based on deviation from this reference population. Based on results of the coagulation profile, horses were grouped as having disseminated intravascular coagulation (DIC) or no DIC. DIC was defined as at least 3 abnormal coagulation parameters.⁵ An abnormal coagulation parameter was defined as at least 2 standard deviations (SD) above the mean for PT and aPTT, at least 2SD below the mean for fibrinogen, AT, and platelet count, and FDP exceeding the highest FDP concentration recorded in the reference population. Based on results of the TEG and TF-TEG, horses were grouped as having a coagulopathy of ≥ 1 , 2, or 3 TEG or TF-TEG parameters. A coagulopathy of a TEG or TF-TEG parameter was defined as at least 2SD above or below the mean for all parameters. The direction of change and incidence of abnormality for each parameter were recorded.

Lesion Type

Horses were grouped into 1 of 4 lesion categories: nonstrangulating medical (NSM), nonstrangulating surgical (NSS), strangulating (S), and inflammatory (I). The diagnosis listed in the medical record determined by the clinician managing the case was used to categorize lesion type. Minimum database in horses presenting for gastrointestinal disease included physical examination, nasogastric intubation, rectal examination, PCV and TS, CBC, and blood gas w/ electrolytes with further diagnostics performed at the discretion of the admitting clinician. If available, surgical or necropsy reports were used to confirm the listed diagnosis.

Horses with NSM lesions without evidence of an underlying inflammatory or strangulating lesion on clinical or necropsy evaluation were managed with medical therapy. Horses with NSS lesions without evidence of an underlying inflammatory or strangulating lesion at the time of surgery were managed with surgical exploration and treatment. Horses with S lesions had evidence of obstruction to intestinal perfusion at surgery or necropsy. Necessity for resection

and anastomosis was not required for inclusion in the strangulating category. Horses with inflammatory lesions had evidence of inflammatory intestinal diseases based on the combination of clinical examination (including elevated temperature [$\geq 101.5^{\circ}\text{F}$], large quantities of nasogastric reflux, diarrhea, mucus membrane appearance, transabdominal ultrasound [changes in contents—fluid, changes in wall thickness]), clinical pathology (WBC count [leucopenia, left shift, leukocytosis], abdominocentesis analysis), surgical, or necropsy findings.

SIRS

Horses were classified as having SIRS if they had at least 2 of the following abnormalities on physical examination at presentation: $T \geq 101.5^{\circ}\text{F}$, $\text{HR} \geq 60$ bpm, $\text{RR} \geq 30$ bpm, WBC count $\geq 12,500$ or $\leq 4,500$ cells/ μL , and $\geq 10\%$ band neutrophils. These criteria are an adaptation of SIRS criteria used in foals²⁹ to adult horses.

Complications

Medical records were examined to determine the incidence of the following complications throughout hospitalization: ileus, diarrhea, fever, thrombophlebitis, and laminitis. Ileus was defined as ≥ 8 L reflux single time or ≥ 20 L in 24 hours.³⁰ Diarrhea was defined as liquid feces that were unable to remain on top of shavings. Fever was defined as a temperature of $\geq 101.5^{\circ}\text{F}$. Thrombophlebitis was defined as identification of swelling over a jugular vein with one or more of the following: pain, heat, and/or decreased/absent flow through the vessel. Laminitis was defined as acute lameness with one or more of the following: standing with forelimbs extended in front and the majority of weight-bearing on the hindlimbs, increased digital pulses, increased hoof temperature, clefting at the coronary band, positive to hoof testers, or radiographic findings consistent with laminitis.

Survival

Survival was defined as survival to hospital discharge. Reason for nonsurvival (cost versus prognosis; euthanasia versus death) was not determined.

Statistical Analysis

Statistical analysis was performed by commercial statistical analysis software.¹ Descriptive statistics were performed on the coagulation profiles, TEG, and TF-TEG parameters. Means, standard deviations, and ranges were calculated. Normality was assessed by the Shapiro-Wilk test.

TEG and coagulation profile values were compared for the following groups: horses that survived versus those that did not survive, SIRS versus no SIRS, ileus versus no ileus, diarrhea versus no diarrhea, fever versus no fever, thrombophlebitis versus no thrombophlebitis, and laminitis versus no laminitis. These comparisons were done by a Student's *t*-test if results were normally distributed or with a Wilcoxon's sum-rank test if they were not normally distributed. TEG and coagulation profile values were compared between study horses in different disease groups by ANOVA or Kruskal-Wallis' test depending on data distribution. Significance was set at $P \leq .05$.

The proportions of horses with DIC, TEG coagulopathy, and TF-TEG coagulopathy were compared between horses in the following categories: survival versus no survival, SIRS versus no SIRS, ileus versus no ileus, diarrhea versus no diarrhea, fever versus no fever, thrombophlebitis versus no thrombophlebitis, and laminitis versus no laminitis with Fischer's exact test. The proportions of horses with DIC, TEG coagulopathy, and TF-TEG coagulopathy were compared between horses by lesion type with χ^2 -test. Significance was set at $P \leq .05$.

Results

Study Population

One-hundred and one horses admitted for emergency evaluation of gastrointestinal disease were included in the study. Horses included a variety of breeds (28 Quarter Horses [QH], 16 Thoroughbreds, 15 Warmbloods, 9 Arabian, 7 Paint, 5 Appaloosa, 4 Paso Fino, 4 Pony, 3 Saddlebred, 2 Tennessee Walking Horse, 2 mixed breed, 1 each of 6 other breeds). There were 54 geldings, 41 mares, and 6 stallions. Horses were 1–36 years old (11.9 ± 6.6 years; median 10 years). The 20 healthy adult horses used to determine reference ranges had an average age of 9.5 ± 4.8 years and an age range of 2–20 years. These horses also represented a selection of breeds (15 QH, 2 Paint, 1 each of 3 other breeds) and sex (10 mares, 7 geldings, 3 stallions).

Most horses had received one or more medications as part of their initial treatment and evaluation in the field, and to facilitate examination at admission. Common medications received before referral included, but were not limited to, sedatives (xylazine ~ 0.2 – 1 mg/kg, detomidine ~ 0.005 – 0.02 mg/kg, butorphanol ~ 0.01 – 0.02 mg/kg), non-steroidal anti-inflammatory drugs before referral (flunixin meglumine ~ 1 mg/kg), and fluids administered IV.

Coagulopathy

Six horses met the criteria for DIC. There were 35, 29, and 16 horses that had coagulopathies evidenced as ≥ 1 , 2, and 3 TEG parameters, respectively. There were 42, 22, and 12 horses that had coagulopathies indentified as ≥ 1 , 2, and 3 TF-TEG parameters, respectively (Table 1).

For TEG coagulopathies, CL60 (24 increased) and Ly60 (24 decreased) were the most common parameters affected, followed by K (12 increased), R (10 increased), MA (2 increased, 4 decreased) and Ang (6 decreased), CL30 (1 decreased), and Ly30 (1 increased).

For TF-TEG coagulopathies, Ang was the most common parameter affected (1 increased, 18 decreased), followed by R (15 increased, 3 decreased), K (17 increased), CL60 (15 increased), MA (1 increased, 12 decreased), CL 30 (1 decreased), Ly30 (1 increased), and Ly60 (1 increased).

Lesion Type

There were 34 NSM horses (18 without specific diagnosis, 5 ileal impactions, 4 left dorsal displacements of the large colon, 2 large colon impactions, and 1 each cecal impaction, small colon impaction, jejunal stricture, sand colic, and right dorsal displacement of the large colon), 18 NSS horses (6 right dorsal displacements of the large colon, 3 left dorsal displacements of the large colon, 3 sand impactions, 2 other large colon displacement, and 1 each fecolith, enterolith, ileal impaction with right dorsal displacement of the large colon, and no identified lesion), 26 S horses (9 small intestinal strangulating lipomas, 5 large colon volvuluses, 2 epiploic foramen entrapments, 2 small intestinal volvuluses, 2 small intestinal strangulations within a rent in the omentum, 2 ischemic small intestinal segments of unknown cause, and 1 each gastrosplenic entrapment, mesodiverticular band strangulation of small

Table 1. TEG and TF-TEG in normal horses and resulting definition for coagulopathy of each parameter.

	R (min)	K (min)	Ang (°)	MA (mm)	CL30 (%)	LY30 (%)	CL60 (%)	LY60 (%)
TEG								
Normal	16.2 (5.8)	5.7 (3.7)	42.5 (13.2)	61.7 (8.4)	97.3 (2.0)	0.7 (0.7)	90.3 (3.7)	3.8 (1.7)
Coagulopathy	<4.7	<0 (N/A)	<16.0	<44.8	<93.3	<0 (N/A)	<83.0	<0.3
	>27.8	>13.1	>69.0	>78.6	>100 (N/A)	>2.1	>97.7	>7.3
N	20	20	20	20	18	18	15	15
TF-TEG								
Normal	6.9 (1.3)	3.2 (1.1)	52.8 (7.5)	62.9 (5.2)	97.9 (1.6)	0.5 (0.5)	91.5 (2.85)	3.0 (1.5)
Coagulopathy	<4.4	<1.0	<37.8	<52.6	<94.7	<0 (N/A)	<85.9	<0 (N/A)
	>9.4	>5.4	>67.8	>73.3	>100 (N/A)	>1.6	>97.1	>6.1
N	20	20	20	20	20	20	18	18

Mean (SD).

TEG, thrombelastography; TF-TEG, thrombelastography performed with tissue factor activation; R, reaction time; K, k value; Ang, angle; MA, maximum amplitude; CL, clot lysis; Ly, lysis; 30, 30 minutes after reaching MA; 60, 60 minutes after reaching MA.

intestine, large colon ischemia of unknown cause, and small colon strangulating lipoma), and 23 I horses (6 enteritis, 7 colitis, 6 intestinal rupture, 3 typhlocolitis, and 1 enterocolitis).

TEG-MA was decreased in horses with inflammatory lesions compared with horses with NSM and NSS lesions ($P = .012$) (Table 2). TF-TEG CL-30 and CL-60 were increased in horses with inflammatory lesions compared with horses with NSS lesions ($P = .033$ and $P = .010$) (Table 3). TF-TEG LY-60 was decreased in horses with inflammatory lesions compared with horses with NSS lesions ($P = .011$). One or more TF-TEG coagulopathy was associated with lesion type ($P = .0361$; 9/34 [26.5%] NSM, 7/18 [38.9%] NSS, 11/26 [42.3%] S, 15/23 [65.2%] I). Two or more TF-TEG coagulopathies was associated with lesion type ($P = .0007$; 1/34 [2.9%] NSM, 3/18 [16.7%] NSS, 7/26 [26.9%] S, 15/23 [65.2%] I). TEG coagulopathies and ≥ 3 TF-TEG were not associated with lesion type.

Analysis of coagulation profiles revealed prolongation of PT in I (10.90 ± 1.41 seconds; normal horses: 9.57 ± 0.27 seconds) and S (10.26 ± 0.69 seconds) lesions compared with NSM (9.74 ± 0.50 seconds) lesions ($P = .0005$) and an increase in fibrinogen concentration in horses with I

(385 ± 107 mg/dL, normal horses: 336 ± 62 mg/dL) lesions compared with horses with NSM (301 ± 62 mg/dL) and S (316 ± 122 mg/dL) lesions ($P = .019$ —both). DIC was not associated with lesion type.

SIRS

There was insufficient information in medical records for SIRS classification in 6 horses. Of the remaining 95 horses, 27 horses had evidence of SIRS (1 NSM, 3 NSS, 7 S, 16 I).

TEG MA was decreased in horses with SIRS ($P = .004$) (Table 4). TF-TEG CL30 and CL60 were increased in horses with SIRS ($P = .019$ and $P = .013$). TF-TEG LY30 and LY60 were decreased in horses with SIRS ($P = .020$ and $P = .010$). TEG and TF-TEG coagulopathies were not associated with the presence of SIRS.

Analysis of coagulation profiles revealed a prolongation of PT and aPTT in horses with SIRS (10.97 ± 1.19 and 62.8 ± 12.7 seconds, respectively; aPTT normal horses: 59.0 ± 8.0 seconds) compared with horses without SIRS (9.91 ± 0.56 and 57.2 ± 8.1 seconds, respectively) ($P < .0001$ and $P = .032$). DIC was associated with the presence of SIRS ($P = .005$). All horses with DIC had SIRS.

Table 2. TEG parameters by lesion type in horses with gastrointestinal disease.

	R (min)	K (min)	Ang (°)	MA (mm)	CL30 (%)	LY30 (%)	CL60 (%)	LY60 (%)	CI
Normal	16.2 (5.8)	5.7 (3.7)	42.5 (13.2)	61.7 (8.4)	97.3 (2.0)	0.7 (0.7)	90.3 (3.7)	3.8 (1.7)	6.2 (1.4)
NSM	18.1 (7.6)	6.5 (3.7)	38.2 (12.0)	62.1 (7.9) ^a	99.1 (1.3)	0.2 (0.3)	93.7 (4.1)	1.9 (1.6)	0.1 (2.0)
	8.5–43.9	2.3–17.8	12.6–59.8	46.5–79	94.9–100	0–1.6	83.4–100	0–6.7	–6.0–3.2
N	34	33	33	33	30	30	26	26	33
NSS	18.8 (6.9)	7.5 (4.7)	36.6 (10.9)	62.0 (9.0) ^a	97.8 (2.4)	0.7 (1.1)	93.0 (5.7)	2.7 (2.4)	–0.1 (1.5)
	8.7–34.4	3.3–20.1	15–49.4	42.8–78.6	92.1–100	0–4.6	83.7–100	0–6.8	–3.0–1.5
N	17	17	17	17	17	17	17	17	17
S	17.0 (6.8)	8.4 (9.9)	36.7 (13.8)	59.6 (6.9) ^{a,b}	99.1 (1.3)	0.2 (0.3)	94.6 (3.8)	1.7 (1.5)	–0.7 (3.3)
	10.5–37.2	3.2–46.8	5.7–52.4	45.7–71.1	95.5–100	0–1.2	87.8–100	0–5.2	–13.4–1.7
N	23	23	23	22	21	21	21	21	23
I	18.6 (7.1)	7.8 (4.7)	33.0 (12.9)	54.8 (9.6) ^b	99.2 (1.3)	0.1 (0.3)	95.3 (4.2)	1.5 (1.6)	–1.2 (2.2)
	5.9–36.5	1.8–23.6	10.5–61.4	35.8–70.8	95.8–100	0–1	86.6–100	0–5.3	–5.3–2.3
N	22	22	22	22	22	22	21	21	22

NSM, nonstrangulating medical; NSS, nonstrangulating surgical; S, strangulating; I, inflammatory; TEG, thrombelastography; R, reaction time; K, k value; Ang, angle; MA, maximum amplitude; CL, clot lysis; Ly, lysis; 30, 30 minutes after reaching MA; 60, 60 minutes after reaching MA.

Mean (SD) and range. Superscripts denote significant differences between lesion types ($P < .05$). Normal values given for comparison.

Table 3. TF-TEG parameters by lesion type in horses with gastrointestinal disease.

	R (min)	K (min)	Ang (°)	MA (mm)	CL30 (%)	LY30 (%)	CL60 (%)	LY60 (%)	CI
Normal	6.9 (1.3)	3.2 (1.1)	52.8 (7.5)	62.9 (5.2)	97.9 (1.6)	0.5 (0.5)	91.5 (2.85)	3.0 (1.5)	5.0 (0.8)
NSM	7.1 (1.6) ^a	3.6 (0.8)	48.4 (6.1)	61.0 (5.9)	99.1 (1.2) ^{c,d}	0.2 (0.3)	93.2 (2.7) ^{e,f}	2.1 (1.2) ^{g,h}	2.2 (1.0)
	4.2–11.2	2–5.6	37.5–65	47.9–73.6	95.8–100	0–1.2	88.6–100	0–4.8	0.5–4.7
N	34	34	34	34	30	30	28	28	34
NSS	8.3 (3.5) ^{a,b}	4.1 (1.6)	46.3 (10.3)	61.0 (6.4)	98.6 (1.0) ^c	0.3 (0.3)	92.1 (2.6) ^c	2.6 (1.1) ^g	2.0 (1.0)
	4.6–21.3	1.8–7.3	24.6–60	49.6–71	96.6–100	0–1.1	88.5–99.4	0–4.3	0.2–3.3
N	18	18	18	18	18	18	18	18	18
S	7.5 (2.5) ^{a,b}	4.4 (1.8)	45.0 (8.9)	59.5 (8.0)	99.1 (1.2) ^{c,d}	0.2 (0.3)	94.3 (3.0) ^{e,f}	1.7 (1.3) ^{g,h}	2.0 (1.4)
	4.7–14.9	2.6–9.1	24.5–58	35.2–71.2	95.7–100	0–1.2	87.8–99.7	0–5.1	–2.2–4.3
N	26	26	26	26	25	25	25	25	26
I	8.6 (2.8) ^b	5.1 (2.8)	43.7 (11.7)	56.7 (9.3)	99.3 (1.4) ^d	0.2 (0.4)	95.3 (4.1) ^f	1.5 (1.6) ^h	1.3 (1.5)
	3.2–18.1	1.3–12.3	19.6–69.2	28.8–70.8	94.3–100	0–1.8	86.6–100	0–6.2	–2.5–3.5
N	23	23	23	23	23	23	23	23	23

NSM, nonstrangulating medical; NSS, nonstrangulating surgical; S, strangulating; I, inflammatory; TF-TEG, thrombelastography performed with tissue factor activation; R, reaction time; K, k value; Ang, angle; MA, maximum amplitude; CL, clot lysis; Ly, lysis; 30, 30 minutes after reaching MA; 60, 60 minutes after reaching MA.

Mean (SD) and range. Superscripts denote significant differences between lesion types ($P < .05$). Normal values given for comparison.

Complications

Information available in medical records was sufficient to determine the presence of complications in at least 71 horses. There were 28 horses with complications (17 with 1 complication; 7 with 2 complications; and 4 with 3 complications). There were 14 horses with ileus, 10 horses with diarrhea, 9 horses with fever, 8 horses with thrombophlebitis, and 2 horses with laminitis.

There was no association between the occurrence of ileus and any TEG or TF-TEG parameters or coagulopathies or DIC. Analysis of coagulation profiles revealed a relative prolongation of aPTT in horses with ileus compared with those without (64.4 ± 10.2 versus 57.6 ± 9.8 seconds; $P = .023$).

Analysis of TEG parameters revealed no association with the presence of diarrhea. Analysis of TF-TEG

parameters in horses with diarrhea revealed a relatively decreased CL30 and increased LY30 ($P = .040$ and $.041$, respectively) compared with those without diarrhea. Analysis of coagulation profiles revealed no association with diarrhea. There was no association between the presences of diarrhea and TEG or TF-TEG coagulopathies or DIC.

There was no association between the presence of fever and any TEG, TF-TEG, or coagulation profile parameters.

There was no association between thrombophlebitis and any TEG, TF-TEG, or coagulation profile parameter. The presence of one or more TF-TEG coagulopathies was associated with thrombophlebitis ($P = .018$; 6/8 [75%] thrombophlebitis, 19/64 [30%] no thrombophlebitis). There was no association between ≥ 2 or ≥ 3 TF-TEG coagulopathies, any TEG coagulopathies, or DIC and thrombophlebitis.

Table 4. TEG and TF-TEG parameters in horses with gastrointestinal disease with and without evidence of SIRS.

	R (min)	K (min)	Ang (°)	MA (mm)	CL30 (%)	LY30 (%)	CL60 (%)	LY60 (%)	CI
TEG									
Normal	16.2 (5.8)	5.7 (3.7)	42.5 (13.2)	61.7 (8.4)	97.3 (2.0)	0.7 (0.7)	90.3 (3.7)	3.8 (1.7)	6.2 (1.4)
No SIRS	17.8 (7.2)	7.1 (6.3)	37.9 (12.4)	61.6 (8.0) ^a	98.7 (1.7)	0.3 (0.78)	93.6 (4.3)	2.2 (1.8)	–0.2 (2.5)
	6.6–43.9	1.8–46.8	5.7–61.4	42.8–79.0	92.15–100	0–4.6	83.4–100	0–6.7	–13.4–3.2
N	65	64	64	63	61	61	58	58	65
SIRS	17.6 (5.6)	7.7 (5.6)	34.1 (12.4)	55.9 (8.6) ^b	99.2 (1.5)	0.2 (0.4)	95.1 (4.5)	1.6 (1.8)	–0.8 (1.9)
	5.9–28.6	2.6–25	10.5–57.3	35.8–70.8	94.1–100	0–1.8	84.3–100	0–6.8	–4.8–2.2
N	26	26	26	26	24	24	24	24	26
TF-TEG									
Normal	6.9 (1.3)	3.2 (1.1)	52.8 (7.5)	62.9 (5.2)	97.9 (1.6)	0.5 (0.5)	91.5 (2.85)	3.0 (1.5)	5.0 (0.8)
No SIRS	7.6 (2.6)	4.0 (1.5)	46.6 (8.8)	60.2 (6.7)	98.8 (1.3) ^c	0.2 (0.4) ^c	93.0 (2.9) ^g	2.2 (1.3) ⁱ	2.0 (1.1)
	3.2–21.3	1.3–9.1	24.5–69.2	35.2–73.6	94.3–100	0–1.8	86.6–100	0–6.2	–2.2–4.7
N	68	68	68	68	63	63	62	62	68
SIRS	8.1 (2.6)	4.3 (1.6)	46.6 (8.8)	58.7 (7.4)	99.5 (0.8) ^d	0.1 (0.2) ^f	95.0 (3.5) ^h	1.4 (1.2) ^j	1.7 (1.2)
	3.7–18.1	2.6–10.9	25–58	40.7–10.8	96.6–100	0–0.9	88.8–100	0–4.4	–1.2–3.6
N	27	27	27	27	27	27	26	26	27

TEG, thrombelastography; TF-TEG, thrombelastography performed with tissue factor activation; R, reaction time; K, k value; Ang, angle; MA, maximum amplitude; CL, clot lysis; Ly, lysis; 30, 30 minutes after reaching MA; 60, 60 minutes after reaching MA; SIRS, systemic inflammatory response syndrome.

Mean (SD) and range. Superscripts denote significant differences between SIRS and No SIRS ($P < .05$). Normal values given for comparison.

Analysis of TEG parameters in horses that developed laminitis revealed a relative decrease in MA, CL60, and CI ($P = .004$, $.045$, and $.036$, respectively) compared with those without laminitis. Analysis of TF-TEG parameters revealed a decrease in MA and CI ($P = .019$ and $.019$, respectively) in horses with laminitis compared with those without laminitis. Analysis of coagulation profiles revealed no association with laminitis. There was no association between TEG coagulopathies, TF-TEG coagulopathies, or DIC and laminitis.

Survival

Twenty-one horses did not survive to discharge. TEG R, K, CL30, and CL60 were increased in nonsurvivors ($P = .007$, $.004$, $.037$, and $.050$, respectively) (Table 5). TEG Ang, MA, Ly30, Ly60, and CI were decreased in nonsurvivors ($P = .0003$, $.006$, $.042$, $.027$, and $.0004$, respectively). TF-TEG R, K, CL30, and CL60 were increased in nonsurvivors ($P = .037$, $.004$, $< .0001$, and $< .0001$, respectively). TF-TEG Ang, Ly30, Ly60, and CI were decreased in nonsurvivors ($P = .005$, $.0002$, $< .0001$, and $.043$, respectively). The presence of 2 or more TEG coagulopathies (11/21 [52.4%] nonsurvivors; 18/80 [22.5%] survivors; $P = .013$), ≥ 3 TEG coagulopathies (7/21 [33.3%] nonsurvivors; 9/80 [11.3%] survivors; $P = .038$), ≥ 1 TF-TEG coagulopathies (15/21 [71.4%] nonsurvivors; 27/80 [33.8%] survivors; $P = .003$), and ≥ 2 TF-TEG coagulopathies (11/21 [52.4%] nonsurvivors; 11/80 [13.8%] survivors; $P = .0004$) were associated with nonsurvival. There was no association between ≥ 1 TEG coagulopathies or ≥ 3 TF-TEG coagulopathies and survival.

Analysis of coagulation profiles revealed a prolongation of PT and aPTT in nonsurvivors (11.19 ± 1.51 and 64.8 ± 12.0 seconds, respectively) compared with survivors (10.01 ± 0.72 and 57.9 ± 9.3 seconds, respectively)

($P < .0001$ and $P = .021$, respectively). The presence or absence of DIC was not associated with survival.

Discussion

The findings of this study support our hypotheses that TEG performed at admission identified abnormalities associated with inflammatory lesions, SIRS, the development of diarrhea, thrombophlebitis, laminitis, and fatality. The directions of change of TEG parameters were consistent with hypocoagulation and hypofibrinolysis. Depending on the balance within the horse, this could result in tendencies toward bleeding or thrombosis. No single parameter or number of coagulopathies identified with TEG appears ideal for predicting outcome of horses with colic.

Traditional coagulation testing in horses with gastrointestinal disease performed in previous studies revealed evidence of consumption of coagulation factors manifested by prolongation of coagulation times.^{2,4,6,8,11-15} Prolongation of coagulation times is likely secondary to activation and subsequent consumption of coagulation factors. Once activation and consumption have begun, whether a patient is hypercoagulable or hypocoagulable depends on the balance between the two and cannot be determined by traditional coagulation testing. In our population, horses with severe gastrointestinal disease have progressed to hypocoagulation, based on TEG analysis, by the time of presentation.

Horses with gastrointestinal disease have an increase in products of fibrinolysis with a concurrent decrease in plasminogen, which is most consistent with prior activation and consumption of fibrinolytic enzymes.^{2,4,8,19} Additionally, increases in inhibitors of fibrinolysis have been identified.^{9,16} Inflammation in other species increases inhibition of fibrinolysis by several mechanisms.^{31,32} These findings suggest that the hypofibrinolysis identified by

Table 5. TEG and TF-TEG parameters in surviving and nonsurviving horses with gastrointestinal disease.

	R (min)	K (min)	Ang (°)	MA (mm)	CL30 (%)	LY30 (%)	CL60 (%)	LY60 (%)	CI
TEG									
Normal	16.2 (5.8)	5.7 (3.7)	42.5 (13.2)	61.7 (8.4)	97.3 (2.0)	0.7 (0.7)	90.3 (3.7)	3.8 (1.7)	6.2 (1.4)
Survivor	17.1 (65) ^a	6.4 (3.9) ^c	38.6 (11.5) ^c	61.0 (8.2) ^g	98.7 (1.7) ^j	0.3 (0.7) ^k	93.7 (4.3) ^m	2.1 (1.8) ^o	0.03 (1.8) ^q
	6.6–43.9	1.8–25	11.5–61.4	35.8–79.0	92.1–100	0–4.6	83.4–100	0–6.8	–6.0–3.2
N	77	76	76	76	73	73	69	69	77
Non-Survivor	21.9 (8.2) ^b	11.7 (10.3) ^d	27.3 (12.4) ^f	54.8 (9.3) ^h	99.6 (0.9) ⁱ	0.1 (0.2) ^l	96.1 (4.4) ⁿ	1.1 (1.5) ^p	–2.3 (3.3) ^r
	5.9–37.2	3.2–46.8	5.7–59.3	38.9–71.1	96.7–100	0–0.7	87.6–100	0–4.6	–13.4–1.9
N	19	19	19	18	17	17	16	16	19
TF-TEG									
Normal	6.9 (1.3)	3.2 (1.1)	52.8 (7.5)	62.9 (5.2)	97.9 (1.6)	0.5 (0.5)	91.5 (2.85)	3.0 (1.5)	5.0 (0.8)
Survivor	7.3 (1.7) ^a	4.0 (1.6) ^c	47.42 (8.9) ^e	60.2 (7.1)	98.8 (1.3) ^g	0.2 (0.4) ⁱ	93.0 (2.9) ^k	2.3 (1.3) ^m	2.1 (1.2) ^o
	3.2–12.2	1.3–11.8	19.6–69.2	28.8–73.6	94.3–100	0–1.8	86.6–100	0–6.2	–2.5–4.7
N	80	80	80	80	75	75	74	74	80
Non-Survivor	9.3 (4.3) ^b	5.3 (2.4) ^d	41.1 (8.6) ^f	57.6 (8.9)	99.9 (0.3) ^h	0.0 (0.0) ^j	97.0 (2.5) ^l	0.7 (0.7) ⁿ	1.3 (1.4) ^p
	3.7–21.3	2.6–12.3	25–56.4	40.7–71	98.9–100	0–0.2	91.3–100	0–2.7	–1.2–3.6
N	21	21	21	21	21	21	20	20	21

TEG, thrombelastography; TF-TEG, thrombelastography performed with tissue factor activation; R, reaction time; K, k value; Ang, angle; MA, maximum amplitude; CL, clot lysis; Ly, lysis; 30, 30 minutes after reaching MA; 60, 60 minutes after reaching MA.

Mean (SD) and range. Superscripts denote significant differences between survivors and nonsurvivors ($P < .05$). Normal values given for comparison.

TEG in this study could be because of a combination of consumption of fibrinolytic enzymes and increased inhibition of fibrinolysis.

Although TEG appears capable of identifying coagulopathies associated with severe gastrointestinal disease, it is important to note that variability in tracings was observed in the healthy horses and horses with gastrointestinal disease. Additionally, there was marked overlap in the ranges of values for most parameters between horses in different categories. This variability is similar to that previously reported in healthy horses.^{25,26} Thus, interpretation of single TEG tracing in a diseased horse is difficult. It is possible that comparison of serial TEG tracings performed in the same horse could lead to more accurate conclusions.

In an attempt to reduce the impact of the variability, horses were categorized by the number of parameters that were outside of the reference range. No single number of abnormalities was found to best for predicting outcome. Although it would seem logical that an increasing number of abnormalities would be more likely to be associated with morbidity and case fatality rate, this was not this case for lesion type, thrombophlebitis, or survival. This finding is difficult to explain. Given that 5% of normal horses would fall outside of the range of values we used to determine coagulopathies, it might be that horses with multiple abnormalities are more likely to be the horses that would be outliers under normal conditions.

In healthy horses and horses with gastrointestinal disease, variability of most parameters is decreased when TEG is performed with TF (data from current study not presented).²⁵ Although the decreased variability in TF-TEG should make differences between groups easier to identify, this was not obvious in the current study. This could be because of the coagulation abnormality being obscured by the procoagulant activity of added TF. This could be particularly true in horses with gastrointestinal disease because they have lower concentrations of factor VII.¹¹

Several limitations of this study should be considered when interpreting the results. There were a small number of horses with complications (laminitis [$n = 2$]) in this study. Thus, the study may be underpowered to identify any associations between coagulopathies and complications and results should be interpreted with caution. Additionally, no attempt was made to analyze the effect of interactions between TEG parameters (ie, horses with increased R are likely to have increased K) or groups (ie, horses with inflammatory lesions are likely to have SIRS).

Another limitation of the study is that horses that did not survive were not separated based on the reason the owner elected euthanasia because of a poor prognosis versus financial limitations. However, 20/21 horses that were euthanized had a poor prognosis evidenced by a diagnosis of severe disease at surgery or necropsy, diagnosis of gastrointestinal rupture on abdominocentesis, and failure of aggressive medical treatment, surgical treatment, or both. Additionally, the inclusion of horses euthanized for financial limitations results in horses with less severe disease—and likely less severe coagulopathies—in the nonsurvivor group could decrease the likelihood to identify coagulopathies associated with survival.

Another limitation of the study is lack of control for the potential effect of therapies administered before referral and between admission and sampling. Horses that were treated with medications with the most well-documented effects on coagulation, synthetic colloids and plasma, were excluded. NSAID administration can affect platelet function and coagulation.^{33–35} Nonselective cyclooxygenase inhibitors have minimal effect on TEG in humans and dogs.^{35,36} Flunixin meglumine and phenylbutazone are therefore unlikely to have a clinically important impact on TEG. The effects of sedatives, fluid administration, or both on coagulation are unknown.

The findings of this study indicate that TEG identifies changes in coagulation and fibrinolysis associated with lesion type, SIRS, morbidity, and fatality in horses with gastrointestinal disease more frequently than traditional coagulation tests. Abnormalities in TEG and TF-TEG parameters were indicative of hypocoagulation and hypofibrinolysis and suggest a consumptive coagulopathy. However, the interhorse variability of TEG tracings makes interpretation and clinical use of the test difficult.

Footnotes

^a Dunkel B, Chan D, Monreal L. Association between hypercoagulability and decreased survival in horses with ischemic or inflammatory gastrointestinal disease. *J Vet Emerg Crit Care* 2010;20:18 (abstract).

^b Abbott N, Chicago, IL

^c Monoject, Covidien, Mansfield, MA

^d Vacutainer, Becton Dickinson, Franklin Lakes, NJ

^e TEG 5000, Haemoscope, Niles, IL

^f v. 4.2.95, Haemoscope

^g Bayer Advia 120, Seimen's Healthcare Diagnostics Incorporated, Deerfield, IL

^h Heska CBC-Diff, Heska Corp, Loveland, CO

ⁱ ACL 1000, Beckman-Coulter, Miami, FL

^j AMAX, Trinity Biotech USA, St Louis, MO

^k Thrombo-Wellcotest, Remel, Atlanta, GA

^l SAS V 9.2, SAS Institute Inc, Cary, NC

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